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DOCKET NO.: BMS-2442/DM-7007 **PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Shuang Liu **Confirmation No.: Not Yet Assigned**

Application No.: 10/663,090 **Group Art Unit: Not Yet Assigned**

Filing Date: September 15, 2003 **Examiner: Not Yet Assigned**

For: MACROCYCLIC CHELANTS FOR METALLOPHARMACEUTICALS

DATE OF DEPOSIT: December 11, 2003

I HEREBY CERTIFY THAT THIS PAPER IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS FIRST CLASS MAIL, POSTAGE PREPAID, ON THE DATE INDICATED ABOVE AND IS ADDRESSED TO THE UNITED STATES PATENT AND TRADEMARK OFFICE, P.O. BOX 1450, ALEXANDRIA, VA 22313-1450.

Elizabeth A. McLoud

TYPED NAME: Elizabeth A. McLoud

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Pursuant to 37 CFR § 1.56 and in accordance with 37 CFR §§ 1.97-1.98, information relating to the above-identified application is hereby disclosed. Inclusion of information in this statement is not to be construed as an admission that this information is material as that term is defined in 37 CFR § 1.56(b).

☒ In accordance with § 1.97(b), since this Information Disclosure Statement is being filed either within three months of the filing date of the above-identified application, within three months of the date of entry into the national stage of the above identified application as set forth in § 1.491, before the mailing date

of a first Office Action on the merits of the above-identified application, or before the mailing date of a first Office Action after the filing of request for continued examination under § 1.114, no additional fee is required.

☐ In accordance with § 1.129(a), this Information Disclosure Statement is being filed in connection with ☐ the first or ☐ second After Final Submission, therefore:

☐ Certification in Accordance with § 1.97(e) is attached; or

☐ The fee of **$180.00** as set forth in § 1.17(p) is attached.

☐ In accordance with § 1.97(c), this Information Disclosure Statement is being filed after the period set forth in § 1.97(b) above but before the mailing date of either a Final Action under § 1.113 or a Notice of Allowance under § 1.311, or before an action that otherwise closes prosecution in the application, therefore:

☐ Certification in Accordance with § 1.97(e) is attached; or

☐ The fee of **$180.00** as set forth in § 1.17(p) is attached.

☐ In accordance with § 1.97(d), this Information Disclosure Statement is being filed after the mailing date of either a Final Action under § 1.113 or a Notice of Allowance under § 1.311 but before, or simultaneously with, the payment of the Issue Fee, therefore included are: Certification in Accordance with § 1.97(e); and the submission fee of **$180.00** as set forth in § 1.17(p).

☐ Copies of each of the references listed on the attached Form PTO-1449 are enclosed herewith.

☒ Copies of references listed on the attached Form PTO-1449 are enclosed herewith

☒ Copies of references listed on the attached Form PTO 1449 are not required to be submitted pursuant to the June 30,. 2003 recent revisions to 37 CFR § 1.98(a)(2)(i).

EXCEPT THAT:

☒ In view of the voluminous nature of references 3, 4, 6, 19, 20, 21, 43, , and the likelihood that these references are available to the Examiner, copies are not enclosed herewith.

☒ In accordance with § 1.98(d), copies of the following references listed on the attached Form PTO-1449 are not enclosed herewith because they were previously cited by or submitted to the U.S. Patent and Trademark Office in patent application(s) for which a claim for priority under 35 U.S.C.§ 120 have been made in the instant application:

☒ Copies of references **53, 72-75** listed on the attached Form PTO-1449 were previously cited by or submitted to the Patent and Trademark Office in prior Application No. **09/660,377**, filed **September 12, 2000**.

Please charge any deficiency or credit any overpayment to Deposit Account No. 23-3050. This form is submitted in duplicate.

☐ The relevance of those listed references which are not in the English language is as follows:

☒ There are no listed references which are not in the English language.

Date: 12/11/03

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Form PTO-1449 Modified List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office	Docket No. BMS-2442/ DM-7007 DIV	Application No. 10/663,090
	Applicant Shuang Liu	
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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)		
	1	Arap, W., et al., "Cancer treatment by targeted drug delivery to tumor vasculature in a mouse model," *Science*, January 16, **1998**, *279*, 377-380
	2	Berning, D.E., et al., "Chemical and biomedical motifs of the reactions of hydroxymethylphosphines with amines, amino acids, and model peptides," *J. Am. Chem. Soc.*, **1999**, *121*, 1658-1664
*	**3**	Bodanszky, "Peptide Chemistry: A Practical Textbook," *Springer-Verlag, New York*, **1988**
*	**4**	Bodanszky, et al., "The Practice of Peptide Synthesis," *Springer-Verlag, New York*, **1984**
	5	Bousquet, J.-C., et al., "Gd-DOTA: characterization of a new paramagnetic complex,"*Radiology*, March **1988**, *166(3)*, 693-698
*	**6**	Brinkley, M., *Bioconjugate Chem.*, **1992**
	7	Burgess, K., et al., Synthesis and solution conformation of cyclo[RGDRGD]: a cyclic peptide with selectivity for the αVβ3 receptor," *J. Med. Chem.*, **1996**, *39*, 4520-4526
	8	Burke, T.R., Jr., "Protein-tyrosine kinase inhibitors," *Drugs of the Future*, **1992**, *17(2)*, 119-131
	9	Chang, C.-J., et al., "Protein-tyrosine kinase inhibition: mechanism-based discovery of antitumor agents," *J. of Nat. Prod.*, November **1992**, *55(11)*, 1529-1560
	10	Cheung, S.T., et al., "N-methylamino acids in peptide synthesis. V. The synthesis of N-tert-butyloxycarbonyl,N-methylamino acids by *N*-methylation," Can. *J. Chem.*, **1977**, *55*, 906-910
EXAMINER		**DATE CONSIDERED**

* Copies of these references will not be forwarded to the U.S. Patent and Trademark Office since they are believed to be too voluminous and easily obtainable by the Examiner.

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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)		
	11	Corbett, J.W., et al., "Solid-phase synthesis of a selective α,β_3 integrin antagonist library," *Biorg.& Med. Chem. Letts.*, **1997**, *7(11)*, 1371-1376
	12	Cosic, I., et al., "*In vitro* inhibition of the actions of basic FGF by a novel 16 amino acid peptide," Molecular *and Cell. Biochem.*, **1994**, *130*, 1-9
	13	DeGrado, W.F., et al., "Polymer-bound oxime esters as supports for solid-phase peptide synthesis. Preparation of protected peptide fragments," *J. Org. Chem.*, **1980**, *45*, 1295-1300
	14	Dougher, A.M., et al., "Identification of a heparin binding peptide on the extracellular domain of the KDR VEGF receptor," *Growth Factors*, **1997**, *14*, 257-268
	15	Fischman, A.J., et al., "Infection imaging with technetium-99m-labeled chemotactic peptide analogs," *Semin. Nuc. Med.*, April **1994**, *24(2)*, 154-168
	16	Freidinger, R.M., et al., "Synthesis of 9-fluorenylmethyloxycarbonyl-protected *N*-alkyl amino acids by reduction of oxazolidinones," *J. Org. Chem.*, **1983**, *48*, 77-81
	17	Fry, D.W., "Protein tyrosine kinases as therapeutic targets in cancer chemotherapy and recent advances in the development of new inhibitors," *Exp. Opin. Invest. Drugs*, **1994**, *3(6)*, 577-595
	18	Gho, Y.S., et al., "Development of antiangiogenin peptide using a phage-displayed peptide library," *Cancer Research*, September 1, **1997**, *57*, 3733-3740
*	**19**	Greene, "Protective Groups in Organic Synthesis," *John Wiley & Sons, New York,* **1981**
*	**20**	Greene, "The Peptides: Analysis, Synthesis, Biology," *Academic Press, New York,* **1981**, *Vol. 3*

EXAMINER	**DATE CONSIDERED**

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*	**21**	Gross, et al. (Eds.), "The Peptides: Analysis, Synthesis, Biology," *Academic Press, New York,* **1980-1987**, *Vol. 1, 2, 3, 5, and 9*
	22	Hartman, G.D., et al., "Non-peptide fibrinogen receptor antagonists. 1. Discovery and design of exosite inhibitors," *J. Med. Chem.*, **1992**, *35*, 4640-4642
	23	Haubner, R., et al., "Stereoisomeric peptide libraries and peptidomimetics for designing selective inhibitors of the $\alpha_v\beta_3$ integrin for a new cancer therapy," *Angew. Chem. Int. Ed. Engl.*, **1997**, *36*, 1374-1389
	24	Jardines, L., et al., "neu(c-er*b*B-2/HER2 and the epidermal growth factor receptor (EGFR) in breast cancer," *Pathobiology*, **1993**, *61*, 268-282
	25	Kolinski, R.A., et al., "Ring inversion in plycyclic tetraamines," *Tetrahedron Letts.*, **1981**, *22(23)*, 2217-2220
	26	Maier, L., et al., "Organische phosphorverbindungen 72 Herstellung und eigenschaften von bis(N-hydroxycarbonylmethylamino-methyl)phosphinsäure, $(HO_2CCH_2NHCH_2)_2P(O)OH$, und derivaten," *Phospharus and Sulfur*, **1980**, *8*, 67-72 (English abstract)
	27	Margerstadt, M., et al., "Gd(DOTA): An alternative to Gd(DTPA) as a $T_{1,2}$ relaxation agent for NMR imaging or spectroscopy," *Magn. Reson. Med.*, **1986**, *3*, 808-812
	28	Märkl, V.G., et al., "1,5-diaza-3.7-diphospha-cyclooctane," *Tetrahedron Letts.*, **1980**, *21*, 1409-1412
	29	Merrifield, R.B., "Solid phase peptide synthesis, I. The synthesis of a tetrapeptide," *J. Am. Chem. Soc.*, **1963**, *85*, 2149-2154
	30	Nanda, K.K., et al., "Magneto-structure correlations in macrocyclic dinicke(II) complexes: tuning of spin exchange by varying stereochemistry and auxiliary ligands," *Inorg. Chem.*, **1994**, *33*, 1188-1193

EXAMINER	**DATE CONSIDERED**

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		OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)
	31	Ortega, N., et al., "Systemic activation of the vascular endothelial growth factor receptor KDR/flk-1 selectively triggers endothelial cells with an angiogenic phenotype," *Amer. J. of Pathol.*, November **1997**, *151(5)*, 1215-1224
	32	Ösapay, G., et al., "synthesis of tyrocidine A: use of oxime resin for peptide chain assembly and cyclization," *Tetrahedron Letts.*, **1990**, *31(43)*, 6121-6124
	33	Pierschbacher, M.D., et al., "Influence of stereochemistry of the sequence Arg-Gly-Asp-Xaa on binding specificity in cell adhesion," *J. of Biol. Chem.*, December 25, **1987**, *262(36)*, 17294-17298
	34	Remington's Pharmaceutical Sciences, 17th Ed., *Mack Publishing Co., Easton, PA*, **1985**, page 1418
	35	Rewcastle, G.W., et al., "Tyrosine kinase inhibitors. 5. Synthesis and structure – activity relationships for 4-[(phenylmethyl)amino]- and 4-(phenylamino)quinazolines as potent adenosine 5'-triphosphate binding site inhibitors of the tyrosine kinase domain of the epidermal growth factor receptor," *J. Med. Chem.*, **1995**, *38*, 3482-3487
	36	Roberts, D.C., et al., "Unusual amino acids in peptide synthesis," *The Peptides Analysis, Synthesis, Biology*, Gross, E., et al. (Eds.), **1983**, *Vol. 5, Chap.* 6, 341-449
	37	Runge, V.M., et al., "MR imaging of rat brain glioma: Gd-DTPA versus Gd-DOTA," *Radiology*, **1988**, *166*, 835-838
	38	Senger, D.R., et al., "Angiogenesis promoted by vascular endothelial growth factor: regulation through $\alpha_1\beta_1$ and $\alpha_2\beta_1$ integrins," *Proc. Natl. Acad. Sci. USA*,December **1997**, *94*, 13612-13617
	39	Singh, P.R., et al., "Transition metal chemistry of main group hydrazides. Part 3: Carboxylate appended phosphorus hydrazides as novel functionalized chelating systems. Synthesis and characterization of new cyclometallaphosphohydrazides. X-ray structure of a palladium(II) representative," *Inorg. Chem.*, **1994**, *33*, 736-741
	40	Singh, P.R., et al., "Transition metal chemistry of main group hydrazides, Part 14: Evaluation of new Tc-99m chelates of thiol functionalized phosphorus hydrazides," *Nucl. Med. Biol.*, **1995**, *22(7)*, 849-857

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	41	Soker, S., et al., "Inhibition of vascular endothelial growth factor (VEGF)-induced endothelial cell proliferation by a peptide corresponding to the exon 7-encoded domain of $VEGF_{165}$," *J. of Biol. Chem.*, **1997**, *272(50)*, 31582-31588
	42	Srivatsa, S.S., et al., "Selective α v β 3 integrin blockade potently limits neointimal hyperplasia and lumen stenosis following deep coronary arterial stent injury: evidence for the functional importance of integrin α v β 3 and osteopontin expression during neointimal formation," *Cardiovascular Res.*, **1997**, *36*, 408-428
*	**43**	Steward, et al., "Solid Phase Peptide Synthesis," 2nd ed., *Pierce Chemical Co., Rockford, IL*, **1984**
	44	Taliaferro, C.H., et al., "New multidentate ligands. 22. *N,N'*-dipyridoxylethylenediamine-*N,N'*-diacetic acid: a new chelating ligand for trivalent metal ions," *Inorg. Chem.*, **23**, 1188-1192
	45	Thompson, A.M., et al., "Tyrosine kinase inhibitors. 13. Structure – activity relationships for soluble 7-substituted 4-[(3-bromophenyl)amino]pyrido[4,3-*d*]pyrimidines designed as inhibitors of the tyrosine kinase activity of the epidermal growth factor receptor," *J. Med. Chem.*, **1997**, *40*, 3915-3925
	46	Tramotini, M., et al., "Titrahedron Report Number 271," *Tetrahedron*, **1990**, 1791-1827
	47	Tramotini, M., "Advances in the Chemistry of mannich bases," *Synthesis*, December **1976**, 703-775
	48	Tran, T.-A., et al., "A novel RGD containing dodecapeptidomimetic which exhibits selective binding to the $\alpha_v\beta_3$ receptor," *Bioorg. & Med. Chem. Lett.*, **1997**, *7(8)*, 997-1002
	49	Varga, T.R., "Synthesis of bis(aminomethyl)-phosphinic acids via a mannich reaction," *Synthetic Communication*, **1997**, *27(17)*, 2899-2903
	50	Weisman, G.R., et al., "Tetracyclic tetraamines by glyoxal-macrocyclic tetraamine condensation," *Tetrahedron Letts.*, **1980**, *21*, 335-338

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	51	Wu, P.-L., et al., "1-acyl-2-alkylhydrazines by the reduction of acylhydrazones," *Synthesis*, April **1995**, 435-438
	52	Yayon, A., et al., "Isolation of peptides that inhibit binding of basic fibroblast growth factor to its receptor from a random phage-epitope library," *Proc. Natl. Acad. Sci. USA*, November **1993**, *90*, 10643-10647

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U. S. PATENT DOCUMENTS

Examiner Initial		Document No.	Date	Name	Class	Subclass
	53	5,730,787	03/24/98	Kasai		
	54	4,427,646	01/24/84	Olexa, et al.	424	1.1
	55	4,578,079	03/25/86	Ruoslahti, et al.	623	11
	56	4,792,525	12/20/88	Ruoslahti, et al.	435	240.243
	57	5,086,069	02/04/92	Klein, et al.	514	399
	58	5,087,440	02/11/92	Cacheris, et al.	424	9
	59	5,155,215	10/13/92	Ranney	534	16
	60	5,217,705	06/08/93	Reno, et al.	424	1.1
	61	5,270,030	12/14/93	Vogel, et al.	424	9
	62	5,277,892	01/11/94	Rhodes	424	1.69
	63	5,279,812	01/18/94	Krstenansky, et al.	424	1.1
	64	5,536,814	07/16/96	Ruoslahti, et al.	530	329
	65	5,766,591	06/16/98	Brooks, et al.	424	184.1
	66	5,767,071	06/16/98	Palladino, et al.	514	11
	67	5,770,565	06/23/98	Cheng, et al.	514	11
	68	5,780,426	07/14/98	Palladino, et al.	514	9

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U. S. PATENT DOCUMENTS

Examiner Initial		Document No.	Date	Name	Class	Subclass
	69	5,792,444	08/11/98	Fischman, et al.	424	1.69
	70	5,879,657	03/09/99	DeGrado, et al.	424	1.69
	71	5,880,281	03/09/99	Argese, et al.	540	474

FOREIGN PATENT DOCUMENTS

Examiner Initial		Document No.	Date	Country	Translation YES	Translation NO
	X 72	WO 88/07048	09/22/88	PCT		
	X 73	WO 94/03464	02/17/94	PCT		
	X 74	WO 94/26275	11/24/94	PCT		
	X 75	WO 95/28968	11/02/95	PCT		
—	76	WO 89/05150	06/15/89	PCT		
—	77	WO 89/10135	11/02/89	PCT		

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	78	WO 90/00178	01/11/90	PCT		
	79	WO 90/03391	04/05/90	PCT		
	80	WO 90/15818	12/27/90	PCT		
	81	WO 91/01331	02/07/91	PCT		
	82	WO 91/15515	10/17/91	PCT		
	83	WO 92/13572	08/20/92	PCT		
	84	WO 93/12819	07/08/93	PCT		
	85	WO 93/17719	09/16/93	PCT		
	86	WO 93/23085 √	11/25/93	PCT		
	87	WO 94/00489 √	01/06/94	PCT		
	88	WO 94/05269 √	03/17/94	PCT		
	89	WO 95/14726 √	06/01/95	PCT		
	90	WO 98/15295 √	04/16/98	PCT		
	91	0 398 143 A1 √	11/22/90	EPO		
	92	0 410 537 A1 √	01/30/91	EPO		
	93	0 410 541 A1 √	01/30/91	EPO		
	94	0 422 937 A1 √	04/17/91	EPO		
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FOREIGN PATENT DOCUMENTS

Examiner Initial		Document No.	Date	Country	Translation YES	Translation NO
—	**95**	0 422 938 A1 V	4/17/91	EPO		
	96	0 425 212 A3 V	05/02/91	EPO		
	97	0 478 328 B1 V	04/01/92	EPO		
	98	226,849 A1 V	01/08/25	Great Britain		
	99	2 225 579 A	06/06/90	Great Britain		

EXAMINER	**DATE CONSIDERED**